53. (New) The transgenic mouse of claim 51, wherein the genome comprises a homozygous disruption of the retina-specific nuclear receptor.

54. (New) A cell or tissue isolated from the transgenic mouse of claim 51.

55. (New) A method of producing a transgenic mouse comprising a disruption in an endogenous retina-specific nuclear receptor gene, the method comprising:

(a) introducing a targeting vector which disrupts the endogenous retina-specific nuclear receptor gene in a mouse embryonic stem cell;

(b) selecting the embryonic stem cell whose genome comprises disrupted retina-specific nuclear receptor gene;

(c) introducing the embryonic stem cell of step (b) into a blastocyst;

(d) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse, whose genome comprises a disruption of the retina-specific nuclear receptor gene such that the mouse lacks production of functional retina-specific nuclear receptor and exhibits an eye abnormality.

56. (New) The method of claim 55, wherein the eye abnormality is retinal dysplasia.

REMARKS

I. Amendments

Claims 38-48 and claim 50 are canceled and new claims 51-56 are added. New claims 51-56 do not add new matter and are completely supported by the application as filed, including, for example, at page 2, lines 28-35 and on page 3, lines 13-20.

Amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in related applications. More particularly, the amendments are made solely to expedite prosecution of the subject application and are not intended to limit the scope of the invention. Applicants reserve the right to prosecute any

canceled subject matter at a later time or in a later filed divisional, continuation or continuation-in-part application.

Upon entry of the amendments, claims 51-56 are pending in the instant application. Claim 49 has been allowed. For the Examiner's convenience, claim 49 and claims 51-56 are attached hereto as Exhibit A.

II. Rejections

A. Rejection under 35 U.S.C. § 112, first paragraph

Claims 42-48 were rejected under 35 U.S.C. § 112, first paragraph as not enabling one skilled in the art to make the invention commensurate with the scope of the claim. Applicants respectfully traverse this rejection, however, for the sole purpose of expediting prosecution of the subject application, claims 42-48 have been canceled and replaced with new claims 51-54.

In view of the cancellation of claims 42-48, the rejection under 35 U.S.C. § 112, first paragraph of claims 42-48 is moot, and Applicants request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph. Applicants submit that new claims 51-56 fully comply with the requirements under 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 103

Claims 38-41 and 50 were rejected as being unpatentable under 35 U.S.C. § 103(a) based upon the teachings of Mansour *et al.*, 1988, *Nature* 366:348-352 ("Mansour") in view of Chen *et al.* 1999, *Proc. Natl. Acad. Sci. U.S.A.* 96(26):15149-15154 ("Chen"). Applicants respectfully traverse this rejection, however, for the sole purpose of expediting prosecution, Applicants have canceled claim 38-41 and 50.

In view of the cancellation of claims 38-41 and 50, the rejection under 35 U.S.C. § 112, first paragraph of claims 38-41 and 50 is moot, and Applicants request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph. Applicants submit that new claims 51-56 are not obvious in view of the teachings of Mansour and Chen.

It is believed that the claims are in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-125.

Respectfully submitted,

Date: 01-23-03

Mariette A. Lapiz (Reg. No. 44,202)
DELTAGEN, INC.
740 Bay Road, Redwood City, CA 94063
(650) 569-5100

Enclosures

EXHIBIT A

49. (Allowed) A transgenic mouse comprising a heterozygous disruption in a retina-specific nuclear receptor gene, wherein said disruption in a homozygous state inhibits production of a functional retina-specific nuclear receptor protein resulting in a transgenic mouse exhibiting an eye abnormality.

51. (New) A transgenic mouse whose genome comprises a disruption in an endogenous retina-specific nuclear receptor gene, wherein the transgenic mouse lacks production of functional retina-specific nuclear receptor and exhibits an eye abnormality.

52. (New) The transgenic mouse of claim 51, wherein the eye abnormality is retinal dysplasia.

53. (New) The transgenic mouse of claim 51, wherein the genome comprises a homozygous disruption of the retina-specific nuclear receptor.

54. (New) A cell or tissue isolated from the transgenic mouse of claim 51.

55. (New) A method of producing a transgenic mouse comprising a disruption in an endogenous retina-specific nuclear receptor gene, the method comprising:

(a) introducing a targeting vector which disrupts endogenous retina-specific nuclear receptor gene in a mouse embryonic stem cell;

(b) selecting the embryonic stem cell whose genome comprises disrupted retina-specific nuclear receptor gene;

(c) introducing the embryonic stem cell in step (b) into a blastocyst;

(d) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse, whose genome comprises a disruption of the retina-specific nuclear receptor gene such that the mouse lacks production of functional retina-specific nuclear receptor and exhibits retinal dysplasia.

56. (New) The method of claim 55, wherein the eye abnormality is retinal dysplasia.